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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,518	07/06/2001	Keith D. Allen	R-716	3954

26619 7590 01/13/2005

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EXAMINER
QIAN, CELINE X

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/900,518	ALLEN ET AL.	
	Examiner	Art Unit	
	Celine X Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-36 and 38-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-36 and 38-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 29-36 and 38-41 are pending in the application.

This Office Action is in response to the Amendment filed on 10/12/04.

Response to Amendment

Claims 29-36, 38-41 stand rejected under 35 U.S.C. 101/112 1st paragraph for reasons set forth of the record mailed on 7/13/04 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 101

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 29-36, 38, 39 and newly added claims 40 and 41 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility.

Claims 29-36, 38, 39 and newly added claims 40 and 41 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, substantial and specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Newly added claims 40 and 41 are rejected for same reasons set forth of the record mailed on 7/13/04 and further discussed below.

In response to this rejection, Applicant argues that the examiner's conclusion regarding the ability of the skilled artisan to use the claimed invention is not consistent with the rules regarding the utility of an invention because the claimed invention has a

well-established utility. Applicant assert that the skilled in the art would immediately appreciate how to use a knockout mouse because any knockout mouse has the inherent and well-established utility of defining the function and role of the disrupted gene regardless of specific phenotypes, characterizations or properties of the knockout mouse. Applicant further cites a passage at NIH website which indicate that knockout mice represent a critical tool in studying gene function. Applicant asserts that the knockout mouse have a clear, specific and unquestionable utility as with gas chromatographs, screening assays and nucleotide sequence techniques as taught by MPEP 2107.01,I. Applicant also asserts that the claimed invention is useful for a particular purpose, to study the role of CX2 in light of the observed phenotypes such as increased seizure susceptibility, increased glucose tolerance and increased ability to metabolize glucose. Applicant cites Wang et al., which demonstrate a mouse lacking the SSTR1 or SSTR1 and 5 gene exhibits different diabetic condition. Applicant thus concludes that the claimed mouse is useful because it also exhibits the phenotype of increased glucose tolerance. Lastly, Applicant argues that the utility of the claimed inventions does not depend on a correlation between the disclosed phenotype and a disease in human for the enablement of the claimed invention. Applicant asserts that usefulness in patent law necessarily includes the expectation of further research and development according to *In re Brana*. Applicant also asserts that Prosser reference demonstrates that one skilled in the art would know how to use the claimed mouse which exhibits increased susceptibility to seizure. Furthermore, Applicant asserts that the claimed invention has credible, specific and substantial utility since it can be used to determine gene function. Moreover, Applicant argues that Figure 3 is not representative of the phenotype of the female

knockout mouse that has increased body weight. Applicants thus conclude the claimed invention has well-established utility.

These arguments have been fully considered but deemed unpersuasive. The reasons for the utility and non-enablement rejection were discussed in detail in the office action mailed on 7/13/04. In response to Applicant's response regarding any knockout mouse has a well-established utility, the examiner does not agree with Applicant's assertion that the claimed invention has a well-established utility. Applicant is reminded that in MPEP, the guideline for the utility requirement clearly states: "An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible." In the instant case, the utility that applies to any knockout mouse is not specific to the claimed invention, the CX2 knockout mouse. It was well known to knock out a gene to determine its function or what will happen when the gene is not expressed. However, scientific "utility" is not the same as "patentable utility" or a "well-established" utility. The MPEP and utility guidelines clearly set forth that a "well-established utility" must be specific, substantial and credible. At the time of filing, knockout mice were used for further research in the art. However, further research does not rise to the level of a "well-established utility" because such a utility is not substantial. The utility guidelines specifically state that further research is not a "substantial utility." The following are examples of situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use and, therefore, do not define "substantial utilities": A. Basic research such as studying the properties of the

claimed product itself or the mechanisms in which the material is involved. In this case, further study of mice would have been required to determine how to use the mouse of applicants' invention according to the embodiments described in the specification. Applicant's assertion that the claimed mouse is useful to study the function of CX2 is an invitation for further research on the claimed invention in which the function of said invention Applicant clearly does not know. Further study would be required to determine the function of the disrupted gene. The overall phenotype of the applicant's mice does not correlate to any disorder; therefore, further study would be required to determine how to use the mice to study a disorder, screening drugs and treatment for such disorder. Thus, using the mice claimed for further research is not a "substantial utility."

In response to Applicant's argument that the claimed mouse has same phenotype as the mice cited in Wang et al., Applicant is reminded that the claimed mouse and mouse disclosed in the reference are different products because they have different genetic background and different phenotype. In addition, the prior art teaches that diabetes is caused multiple factors which have nothing to do with the function of CX2 gene. Moreover, the claimed mouse must exhibits additional symptoms such as increased blood glucose level and insulin intolerance, the primary symptoms of human diabetes, for it to be a valid model of diabetes. The specification does not teach such phenotype in the claimed mouse. As such, the claimed mouse is not a valid model of diabetes. Furthermore, the phenotype of increased susceptibility to seizure of the instant claimed mouse is result from the induction of a chemical compound, metrazol. As such, it is unclear what is the functionality of CX2 that contributes to this phenotype because seizure-like behavior is not a direct result from the inhibition of the CX2 gene, rather, it is

result from the induction of a chemical compound, metrazol, which also produces such behavior in wild type mouse. Thus, this phenotype is not specific to the knockout of the CX2 per se, it could involve genes that are unrelated to CX2. As such, the knockout mouse cannot serve as a valid model for seizure. The alleged cited Prosser reference is not included in the Amendment, thus the examiner cannot comment on this reference.

In response to Applicant's argument regard *In re Brana*, the examiner does not agree that it applies in the instant case. Applicant has taken one conclusion out of the context. Although the case law states "Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development," it is referring to a chemical compound for its anti-tumor activity which has been demonstrated in tumor cell line. The specification of that application has taught a substantial and specific use for the claimed compound. However, in the instant case, the claimed knockout mouse does not have a specific and substantial use since the specification does not teach credibly what disease model the claimed mouse represents and/or what type of drug the claimed mouse can screen. Even the female mouse has the phenotype increased body weight, it does not support a well-established utility for said mouse for reasons discussed above. The utility of studying the function of the CX2 is an invitation of further research in which the function of the claimed invention is not known. Therefore, the claimed invention lacks patentable utility and the rejection is maintained.

In response to the 112 1st paragraph rejection, Applicant argues that the phenotype of a mouse with a null allele is predictable because age and gender matched mice are used. Furthermore, Applicant argues that heterozygous mouse can be used to generate

homozygous mouse. Lastly, Applicant asserts that the Crawley reference is not relevant because it discusses strain-to-strain variation in test results, whereas the phenotypic analysis performed by Applicant were based on age, gender and strain matched wild type controls, and these mice are well-suited and commonly used to generate knockout mice. Applicant thus concludes that the claimed mouse is enabled by the instant specification.

These arguments have been fully considered but deemed unpersuasive. The reasons for non-enablement of the invention are discussed in detail in the office action mailed on 7/13/04. Contrary to Applicant's assertion, the phenotype of a mouse with a null is still unpredictable (for detailed reason, see previous office action) even when age and gender matched mice are used because phenotype result from genetic background influence and the specific gene knockout must be distinguished. As such, the phenotype of the claimed mouse is unpredictable. For reasons discussed in the above regarding the lack of utility of the claimed mouse, one skilled in the art would not know how to use the homozygous CX2 mouse. As such, although the heterozygous mouse can be used to make the homozygous mouse, it does not have patentable utility because the homozygous mouse does not have utility. Lastly, the Crawley reference is relevant art to the claimed invention because it discussed strains to strains variation in the art of making and testing the true phenotype of the transgenic knockout mouse, especially the strains C57BL/6 and 129, which is used to make the instant invention according to the specification. Although Applicant use gender, age and strain matched wild type controls, the phenotype of a mutant mouse is not only the result of the targeted gene, but it also reflects interactions with background gene, and other unknown mutations in the genetic background (see pages 107 last paragraph through page 108 1st paragraph). Since two strains commonly

used in ES cell and knockout generation C57BL/6 and various substrains of 129 are unusual on many standard behavioral paradigms (see page 108, 2nd paragraph), further characterization is required to make sure that the claimed phenotype is truly resulted from the inhibition of the CX2 gene. Therefore, for reasons discussed in the previous office action and above, the claimed invention is not enabled.

New Grounds of Rejection Necessitated by Applicant's Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40 and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40 and 41 recites the limitation "said female mouse" in line 1. There is insufficient antecedent basis for this limitation in the claim. The parent claim does not recite a female mouse.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

DAVE TRONG NGUYEN
PRIMARY EXAMINER